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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/324,479	12/02/94	BORDER W	PLA1245

HM12/0225

CATHRYN CAMPBELL
CAMPBELL & FLORES LLP
4370 LA JOLLA VILLAGE DRIVE
SUITE 700
SAN DIEGO CA 92122

EXAMINER	
RABIN, E	
ART UNIT	**PAPER NUMBER**
1644	58

DATE MAILED: 02/25/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 08/349479	Applicant(s) BORDER ET AL.
	Examiner RABIN	Group Art Unit 1644

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Response

A SHORTENED STATUTORY PERIOD FOR RESPONSE IS SET TO EXPIRE -3- MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a response be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for response specified above is less than thirty (30) days, a response within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for response is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to respond within the set or extended period for response will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☒ Responsive to communication(s) filed on 12/31/98.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle,* 1935 C.D. 1 1; 453 O.G. 213.

Disposition of Claims

☒ Claim(s) 21-23 and 25 is/are pending in the application.

Of the above claim(s)_____ is/are withdrawn from consideration.

☐ Claim(s)_____ is/are allowed.

☒ Claim(s) 21-23 and 25 is/are rejected.

☐ Claim(s)_____ is/are objected to.

☐ Claim(s)_____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on_____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on_____ is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number)_____.

☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received:_____.

Attachment(s)

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 54

☐ Interview Summary, PTO-413

☐ Notice of References Cited, PTO-892

☐ Notice of Informal Patent Application, PTO-152

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Other_____

Office Action Summary

DETAILED ACTION

1. The Art Unit location and the Examiner of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1644.

2. Since this application is eligible for the transitional procedure of 37 CFR 1.129(a), and the fee set forth in 37 CFR 1.17(r) has been timely paid, the finality of the previous Office action is hereby withdrawn pursuant to 37 CFR 1.129(a). Applicant's second submission after final filed on December 31, 1998, as Paper No. 57 has been entered.

3. Claim 24 has been canceled. Claims 21-23 and 25 are pending and are currently under examination.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 21-23 and 25 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claim 21 is indefinite for reciting "characterized by". The connotation of "characterized by" is more than mere description; it implies one or more physical steps or procedures to identify the pathology or condition. Therefore, the meaning and scope of the claim is unclear. It is suggested that the claim be changed to recite "pathology or condition wherein".

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

8. Claim 21 stands rejected under 35 U.S.C. § 103 as being unpatentable over Connor *et al.* [J. Clin. Invest. 83: 1661-1666 (May 1989)], for the same reasons as set forth in Paper Nos. 52, 42, and 34.

9. Claims 22 and 23 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Connor *et al.* [J. Clin. Invest. 83: 1661-1666 (May 1989)] as applied to Claim 21 above, and further in view of MacKay *et al.* [J. Clin. Invest. 83: 1160-1167 (Apr 1989)], for the same reasons as set forth in Paper Nos. 52, 42, and 34.

10. Applicant's arguments filed December 31, 1998, as Paper No. 57, have been fully considered, but they are not persuasive.

Applicant argues the rejections of Paragraphs 11 and 12 together (Paper No. 57, Pages 7-10). Applicant argues that the "Rule 131 Declaration, previously submitted on October 1, 1996, with Applicants' Response to Paper No. 42, provides sufficient evidence to antedate the Conner and McKay [*sic*] prior art references relied upon by the Examiner" (Paper No. 57, Page 8).

The Declaration filed on October 7, 1996 as Paper No. 45 under 37 CFR 1.131 has been considered, but is ineffective to overcome the Connor *et al.* and MacKay *et al.* references.

The evidence submitted is insufficient to establish *diligence* from a date prior to the date of reduction to practice of the Connor *et al.* and MacKay *et al.* references to either a constructive reduction to practice or an actual reduction to practice. "When alleging that conception or a reduction to practice occurred prior to the effective date of the reference, the dates in the oath or declaration may be the actual dates or, if the applicant or patent owner does not desire to disclose his or her actual dates, he or she may merely allege that the acts referred to occurred prior to a specified date. *However, the actual dates of acts relied on to establish diligence must be provided* (MPEP § 715.07). See MPEP § 715.07(a) for diligence requirements.

In addition, the scope of the Declaration is not commensurate with the scope of the claims. The data included with the declaration shows the generation of antibodies specific for TGF-β and the inhibition of TGF-β in cell culture. There is no showing indicating that tissues are contacted with the antibodies specific for TGF-β in order to suppress the deleterious accumulation of the TGF-β-induced extracellular matrix.

11. Claims 21-23 and 25 are rejected under 35 U.S.C. § 103 as being unpatentable over Bassols *et al.* [J. Biol. Chem. 263: 3039-3045 (Feb 1988)] in view of Connor *et al.* [J. Clin. Invest. 83: 1661-1666 (May 1989)] and Dasch *et al.* [U.S. Patent 5,571,714 (Nov 1996)].

Bassols *et al.* teach that TGFβ regulates the expression and structure of extracellular matrix chondroitin/dermatan sulfate proteoglycans by elevating the biosynthetic rate of the 45-kDa proteoglycan core protein and by inducing an increase in the molecular mass of the glycosaminoglycan chains (Abstract; Page 3041, Right Column to Page 3043, and Figure 5, in particular). Bassols *et al.* teach that TGFβ regulates proteoglycans in kidney and lung fibroblasts, lung epithelial cells, and preadipocytes (Page 3040, Left Column, Last Paragraph to Paragraph bridging Pages 3040 and 3041, in particular). Bassols *et al.* teach that TGFβ induces kidney fibroblasts to form colonies in semisolid medium (Page 3044, Last paragraph, in particular).

Bassols *et al.* do not teach using anti-TGF-β to inhibit the activity of TGFβ or to inhibit TGF-β-induced scarring. However, Connor *et al.* teach utilizing an anti-TGF-β antibody to treat an *in vitro* model system of intraocular fibrosis, a pathology characterized by extra-cellular matrix accumulation (Page 1661, Column 2, in particular). Connor *et al.* teach *in vivo* usage of anti-TGF-β antibodies to retard or arrest fibrosis (Page 1665, Column 2, in particular). Dasch *et al.* teach that a therapeutically effective amount of the antibody of this invention may be administered to neutralize the biologic activity of TGF-β, which in turn would result in prevention of unwanted fibrosis and that overproduction of TGF-β is associated with interstitial lung fibrosis, liver cirrhosis, and fibrotic skin disorders such as scleroderma and scarring (Column 5, Lines 32-50, in particular). Dasch *et al.* teach that "indications where this mode of treatment is particularly useful are for the control of excessive scar tissue formation, due to surgery or trauma, or prevention of the formation of connective tissue adhesions (Column 6,

Lines 17-20, in particular). Therefore, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to be motivated to use anti-TGF-β antibody to treat the TGF-β-induced fibrotic conditions of Bassols *et al.* and Dasch *et al.* A person of ordinary skill in the art would have been motivated to use anti-TGF-β and would have had ample expectation of success of being able to inhibit the extracellular matrix-inducing activity of TGF-β because of the neutralizing capabilities of anti-TGF-β as taught by Connor *et al.* and by Dasch *et al.* Further, it was a common practice in the art to use neutralizing antibodies to successfully inhibit TGF-β activity. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Double Patenting

12. Applicant has indicated that "the provisional double-patenting rejection of Claims 21-25 over application Serial Nos. 08/407,942 is held in abeyance at this time" (Paper No. 57, Page 2, in particular).

13. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

14. Claims 21-23 and 25 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 27, 30, 35, and 36 of copending Application No. 08/458,864. Although the conflicting claims are not identical, they are not patentably distinct from each other because the two versions of the claims both recite the same method of inhibiting the TGFβ-induced promotion of extracellular matrix production which comprises administering an inhibitor of TGFβ. A grant of a patent on this application would have the effect of prolonging Applicant's term of exclusivity for such embodiments, were the other application to issue first to patent.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 21-23 and 25 are directed to an invention not patentably distinct from Claims 27, 30, 35, and 36 of commonly assigned, copending Application No. 08/ 458,864. Specifically, the claims are not patentably distinct for the reasons set forth above in Paragraph 17.

Commonly assigned, copending Application Nos. 08/ 458,864 discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee is required under 37 CFR 1.78(c) and 35 U.S.C. 132 to either show that the conflicting inventions were commonly owned at the time the invention in this application was made or to name the prior inventor of the conflicting subject matter. Failure to comply with this requirement will result in a holding of abandonment of the application.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g).

15. Claims 21-23 and 25 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 29-30, 33-34, 37-39 and 42 of copending Application No. 08/ 407,942. Although the conflicting claims are not identical, they encompass common subject matter. The claims of the '942 application recite "a method of inhibiting TGFβ-induced accumulation of extracellular matrix ... comprising contacting said tissue with an agent that binds to TGFβ..." The instant claims differ in that they recite "a method of decreasing the deleterious accumulation of extracellular matrix ... comprising ... contacting the tissue with an anti-TGF-β antibody that binds to TGF-β". Although the wording is different, the claims encompass the same generic inventive concept, *i.e.*, inhibition of TGFβ-induced accumulation of extracellular matrix. A grant of a patent on this application would have the effect of prolonging Applicant's term of exclusivity for such embodiments, were the other application to issue first to patent.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

16. Claims 21-23, and 25 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 1-3 of copending Application No. 08/459,865. Although the conflicting claims are not identical, they are not patentably distinct from each other because they encompass common subject matter. The copending claims are directed to methods of "suppressing or treating a pathology characterized by an accumulation of extracellular matrix in a tissue, comprising contacting said tissue with an agent that suppresses the extracellular matrix producing activity of TGFβ". Although the wording of the claims is different, the methods have the same method steps and would achieve the same result, *i.e.*, inhibition of TGFβ-induced accumulation of extracellular matrix. Therefore, the methods are not patentably distinct.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

17. Claims 21-23 and 25 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 13-15 of copending Application No. 08/457,707. Although the conflicting claims are not identical, they are not patentably distinct from each other because the two versions of the claims both recite the same method of treating a pathology characterized by the accumulation of extracellular matrix by administering an agent that inhibits TGFβ.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

18. Claims 13-15 and 19-21 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 1-8, 12-18, and 22 of copending Application No. 08/457,709. Although the conflicting claims are not identical, they are not patentably distinct from each other because they encompass common subject matter. The copending claims are directed to methods of "treating a pathology characterized by an accumulation of extracellular matrix in a tissue, comprising contacting said tissue with an agent that suppresses the extracellular matrix producing activity of TGFβ".

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

19. No claims allowed.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Evelyn Rabin, Ph.D. whose telephone number is (703) 305-6811. The examiner can normally be reached on Monday through Thursday from 7:30 AM to 6:00 PM.

21. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan, can be reached on (703) 308-3973. The FAX number for this Technology Center is (703) 305-3014 or (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technology Center receptionist whose telephone number is (703) 308-0196.

Evelyn Rabin, Ph.D.
Patent Examiner
February 24, 1999

Evelyn Rabin

EVELYN RABIN
PATENT EXAMIN...